Agricultural Lung Diseases

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Agriculture is considered one of the most hazardous occupations. Organic dusts and toxic gases constitute some of the most common and potentially disabling occupational and environmental hazards. The changing patterns of agriculture have paradoxically contributed to both improved working conditions and increased exposure to respiratory hazards. Animal confinement operations with increasing animal density, particularly swine confinement, have contributed significantly to increased intensity and duration of exposure to indoor air toxins. Ongoing research has implicated bacterial endotoxins, fungal spores, and the inherent toxicity of grain dusts as causes of upper and lower airway inflammation and as immunologic agents in both grain and animal production. Animal confinement gases, particularly ammonia and hydrogen sulfide, have been implicated as additional sources of respiratory irritants. It has become evident that a significant percentage of agricultural workers have clinical symptoms associated with long-term exposure to organic dusts and animal confinement gases. Respiratory diseases and syndromes, including hypersensitivity pneumonitis, organic dust toxic syndrome, chronic bronchitis, mucous membrane inflammation syndrome, and asthmalike syndrome, result from ongoing acute and chronic exposures. In this review we focus upon the emerging respiratory health issues in a changing agricultural economic and technologic environment. Environmental and occupational hazards and exposures will be emphasized rather than clinical diagnosis and treatment. Methods of prevention, from both engineering controls and personal respiratory perspectives, are also addressed. *Key words*: agricultural health, agriculture, animal confinement, endotoxin, grain dust, lung diseases, organic dusts, respiratory diseases. — *Environ Health Perspect* 108(suppl 4):705–712 (2000).
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Agriculture is a very diverse industry that includes multiple occupational and environmental exposures and widely varying work practices. There are specific respiratory hazards associated with the various commodities and associated work practices (Table 1). Respiratory disease is one of the main chronic conditions among farmers (*1*) and also affects those in agricultural-related industries. For example, respiratory symptoms have been reported in as many as 93% of veterinarians treating swine (*2*). Bioaerosols comprising organic dusts, microorganisms, and bacterial endotoxins, and chemical toxicants from fermentation and bacterial degradation of grain and animal wastes are the major environmental/occupational health hazards commonly encountered by farmers, their families, and other agricultural workers. Inorganic dusts are prevalent but less clinically significant. Exposure to each of these toxicant classes or to a combination of these toxicants constitutes a risk of respiratory injury.

Changes in the size of agricultural operations and incursion of nonfarm families who make their homes in the rural setting have also broadened and increased the opportunity for significant respiratory exposure-related health effects in the rural community. Large, high-density animal confinement and animal processing facilities are notable in this respect. Animal confinement is of particular interest because of the marked changes in animal husbandry leading to longer and more intense exposures to dusts and gases as indoor air exposures. Moreover, these operations, and production farming in general, are relatively unregulated, as the majority have fewer than 10 employees per employer unit and do not come under the Occupational Safety and Health Administration (OSHA) jurisdiction (*3*). All these factors make measurement difficult of the true extent of agricultural-related respiratory injury and morbidity. In addition to the lack of systematic reporting of agricultural respiratory disease, the lack of medical access to healthcare providers in rural areas because of cultural and financial issues leads to significant underreporting.

The application of respiratory protection principles to agriculture is an essential component of the prevention of agricultural respiratory illnesses. When applying the agricultural safety hierarchy and principles of occupational health, engineering controls are emphasized over personal respiratory protection in reducing respiratory hazards. The measurement of airborne dusts, gases, and endotoxins through zone sampling and personal breathing zones is the primary industrial hygiene technique used to determine the specific hazards and the concentrations. This is essential to correct unsafe levels of toxic gases or dusts and to determine the appropriate personal respiratory protection. Ventilation is a key component of decreasing respiratory hazards by increasing fresh air circulating or venting of toxic gases outside (*4,5*). Often, engineering controls are not sufficient, and personal respirators are required to provide additional safeguards. Personal respirators are either atmosphere-purifying filters, such as two-strap dust/mist/fume masks or chemical cartridges that require a tight facial seal, or atmosphere-supplying respirators such as the self-contained breathing apparatus (SCBA). The selection of the appropriate respirator for the conditions encountered and the proper fit is essential for adequate personal respiratory protection and is required by OSHA (*6*). However, production agriculture and field operations with less than 11 employees, which includes the majority of those working in agriculture, are excluded from OSHA safety regulations and appropriate respiratory protection principles are sporadically and intermittently applied.

The agricultural economic and technologic environment is rapidly changing. Currently, it is estimated that up to 5 million people work in U.S. agriculture (*7*). The 1997 agricultural census estimates that individual farms continue to make up 86% of the total farms; 50.3% of farms produce less than $10,000 income, and 3.6% produce over $500,000 per year. Five to ten percent of the agricultural work force is engaged in animal confinement work, with approximately 250,000 working in hog confinement facilities and another 200,000 in poultry confinement (*8*). In 1998 the number of hog operations was 114,380, with facilities with 2,000 or more hogs accounting for 6% of the operations, but 64% of the total number of hogs (*9*). Work in the dairy industry, grain production, and sugar beet and potato industry also involves confined space work where significant exposure to noxious dusts, pesticides, and toxicant gases can occur. Each of these sources of respiratory exposure, alone or in combination, can exert acute and chronic toxicant lung injury.

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Table 1. Agricultural respiratory hazards and diseases.[a]

Categories	Sources	Environments	Conditions
Organic dusts	Grain, hay, endotoxin, silage, cotton, animal feed, animal byproducts, cotton, microorganisms	Animal confinement operations, barns, silos, harvesting and processing operations	Asthma, asthmalike syndrome, ODTS, chronic bronchitis, hypersensitivity pneumonitis (Farmer's Lung)
Inorganic dusts	Silicates	Harvesting/tilling	Pulmonary fibrosis, chronic bronchitis
Gases	Ammonia, hydrogen sulfide, nitrous oxides, methane, CO	Animal confinement facilities, silos, fertilizers	Asthmalike syndrome, tracheobronchitis, silo-filler's disease, pulmonary edema
Chemicals			
Pesticides	Paraquat, organophosphates, fumigants	Applicators, field workers	Pulmonary fibrosis, pulmonary edema, bronchospasm
Fertilizers	Anhydrous ammonia	Application in fields, storage containers	Mucous membrane irritation, tracheobronchitis
Disinfectants	Chlorine, quarternary compounds	Dairy barns, hog confinement	Respiratory irritant, bronchospasm
Others			
Solvents	Diesel fuel, pesticide solutions	Storage containers	Mucous membrane irritation
Welding fumes	Nitrous oxides, ozone, metals	Welding operations	Bronchitis, metal-fume fever, emphysema
Zoonotic infections	Microorganisms	Animal husbandry, veterinary services	Anthrax, Q fever, psittacosis

[a]Adapted from Schenker (*68*) with additional input from the American Thoracic Society (*7*), Von Essen and Donham (*69*), Zjeda and Dosman (*70*), and Donham et al. (*71*).

Dusts

Inorganic

A tractor tilling a field trailed by large plumes of dust is a common sight throughout the rural landscape, but that is not the only method of exposure to inorganic dusts. Diatomaceous earth containing respirable silica is not an uncommon source of respiratory exposure in different agricultural settings and may be a cause of bronchitis in workers processing sugar beets and potatoes in enclosed work spaces. Very high concentrations of inorganic dusts are generated by field activities such as plowing, tilling, haying, and harvesting. The bulk of the inorganic dusts are silicates. These include crystalline silica (quartz) and noncrystalline amorphous silica (diatomite). Newer tractors with enclosed cabs containing air filtration can decrease respirable dust exposure from an average of 2–20 mg/m^3 to 0.1–1 mg/m^3. Inorganic dust can constitute from 15 to 43% of the total dust exposure in grain handling. Manual tree fruit and grape harvesting are associated with inorganic dust levels greater than OSHA permissible levels (*7*). Burning of rice stubble, which contains as much as 12% silica by weight, exposes workers to smoke containing aerosolized silica. Silica is known to cause pneumoconioses consisting of restrictive lung disease and characteristic opacities on chest radiography. California rice farmers had a higher prevalence of abnormal radiographic findings than the general population (*10*). Inorganic dusts, however, do not contribute to agricultural respiratory disease to the same extent as organic dusts. Furthermore, the weathering effects upon respirable quartz dusts generated by agriculture are considered to be less pathogenic than the freshly fractured quartz dust generated by industrial processes such as mining, quarrying, and sandblasting. Diatomaceous silicate inorganic dusts are also considered to have relatively nontoxic pulmonary properties (*7*).

Organic

Grain dust is a complex mixture of components including vegetable product, insect fragments, animal dander, bird and rodent feces, pesticides, microorganisms, endotoxins, and pollens. The primary sources of toxic and allergenic contributors in animal confinement facilities are animal feces, endotoxins, and pollens. These dust particles range in size from < 0.01 to 100 µm, with up to 40% in the respirable range. Respirable dusts, defined as having a median diameter of 4.0 µm or less and hazardous when deposited in the gas-exchange unit area, penetrate to the level of the terminal bronchioles and alveoli, the gas-exchange area (*11*). Respirable dusts in swine confinement range in concentration from 2 to 60% and may reach as high as 40% of the total dust. Dust levels are highest in the finishing buildings (up to 15 mg/m^3) and from 3 to 5 mg/m^3 in the farrowing and nursery buildings (*7*). The median dust level to which poultry workers are exposed was 11.53 mg/m^3 based on personal sampling (*12*). Grain dusts are generated from production, harvest, transfer, storage, and processing procedures. The highest grain dust levels are associated with grain cleaning, with a median level of 72.5 mg/m^3 (*12*). Other high dust-generating environments and work practices include silos, chopping straw for bedding, unloading grain silos, shoveling feed, opening bales of hay for feed, and cleaning old animal housing structures. Under certain conditions organic dusts contain biologically active proteins that may be allergenic and proinflammatory. The biologically active compounds contained in dust, along with coexisting toxicant gases, raise concerns regarding possible additive or synergistic toxic exposures and respiratory health (*8*).

Specific legal standards for acceptable levels of organic dust emissions do not exist. There is very limited monitoring of dust levels in production agricultural settings, as many smaller operations are excluded from routine OSHA inspections. By default, OSHA permissible exposure levels (PELs) for nuisance dusts, particles not otherwise regulated, of 15 mg/m^3 for total dust and 5 mg/m^3 for respirable dust and 10 mg/m^3 for grain dusts (oats, wheat, barley) are used in lieu of a universally accepted upper limit for organic dusts (*13*). The American Government Council of Industrial Hygienists (ACGIH) recommended threshold limit value (TLV) for nuisance dusts is 10 mg/mg^3 inhalable and 3 mg/m^3 respirable (*11*). The National Institute for Occupational Safety and Health (NIOSH) recommended exposure level (REL) for grain dust is 4 mg/mg^3. By contrast investigators such as Donham and Reynolds have determined that dose–response adverse pulmonary effects occur at lower total organic dust levels above 2.4–2.5 mg/m^3 and respirable dust levels of 0.23 mg/m^3 for swine confinement operations and 2.4 mg/m^3 total dust and 0.16 mg/m^3 respirable dust in poultry house operations (*14–16*) (Table 2). The significant levels were determined to be those that caused a 5% decrease in the postshift forced expiratory volume in 1 sec (FEV_1). As a result of these dose–response findings showing a decreased FEV_1 after a work shift, recommendations have been made for the development of new threshold-limit standards to adequately protect workers in the animal confinement industry (*14–16*).

Allergens

Allergens encountered include animal danders in confinement facilities, and allergenic protein components in grain dusts, particularly those from wheat sorghum and soy. Biologic mechanisms involved in the inflammatory response include complement activation, neutrophil chemotactic activity, and increased peripheral blood neutrophil response (*17,18*). Pollens, insect fragments, fungal molds, and bacteria are ubiquitous allergens and can occur at high levels in grain or animal confinement enclosed space settings. Noxious allergenic effects from exposures in enclosed space facilities can vary from simple upper respiratory allergies to bronchial hyperreactivity and asthma. Bronchial hyperreactivity is common among workers in swine confinement facilities (*8*). Reports of wheezing are more common in agricultural workers than reports of physician-diagnosed asthma. These reports may include the non-IgE-induced asthmalike syndrome described later in the respiratory illnesses and syndromes section. Other type I allergens, which account for immediate reactions, include pig epithelium, urine, and saliva (*19*), and animal feed components containing IgE-inducing food proteins. Storage mites of the species *Acarus siro*, *Lepidoglyphys destructor*, and *Gypcyphagus domesticus* have been associated with type I allergic reactions (barn allergy) and are found in warm, humid, and moldy environments (*7,20,21*)

Endotoxins and Inflammation

Intertwined with these allergenic exposure-related effects is the role of bacterial endotoxins generated in these same environments. These heat-stable lipopolysaccharides (LPSs) derived from gram-negative bacteria cell walls can produce flulike symptoms in exposed workers (*5,14*). LPS contains a biologically active lipid (lipid A) presumed to be responsible for the adverse health effects of endotoxins (*5,22*). Endotoxins are measured by *in vitro* biologic assay based upon a Limulus amoebocyte assay and recorded as endotoxin units/cubic meter (EU/m^3) or nanograms/cubic meter (ng/m^3). One EU is roughly equivalent to 0.1 ng/m^3 and is dependent upon the potency of the variety of endotoxin. The endotoxin activity of various gram-negative bacteria varies significantly between species. The genera of gram-negative bacteria that produce endotoxin in agricultural settings include *Pseudomonas, Bacillus, Cornyebacterium, Pasteurella, Vibrio,* and *Enterobacter*. Endotoxins are found where organic dust is produced and raised by animal and human activities. These conditions are found in animal confinement structures (swine and poultry), livestock farming, grain elevators, cotton industry, potato processing, flax industry, and the animal feed industry.

At higher airborne endotoxin concentrations (100–200 ng/m^3), bronchoconstriction can occur in exposed workers. According to the International Commission on Occupational Health, endotoxin concentrations of 1,000–2,000 ng/m^3 can result in organic dust toxic syndrome (ODTS) (*7*). In the experimental setting, it appears that interaction between bacterial/fungal spores and endotoxin can be synergistic in the evolution of ODTS (*22*). Whether endotoxin-mediated pulmonary effects are the prime factors in ODTS is uncertain, as molds and grain dust extract can also contribute to inflammatory pulmonary reactions. Furthermore, endotoxins are implicated as etiologic agents in multiple studies noting deterioration of pulmonary functions or the occurrence of chronic respiratory conditions with evidence of a direct dose–response relationship (*15,16,23–26*). PELs do not exist for endotoxins, but Donham has recommended that 100 EU/m^3 (1,000 ng/m^3) be established as the upper limit of endotoxin values for chronic exposure in swine confinement operations (*14*) (Table 2).

Endotoxins are thought to be the cause of the inflammatory reaction seen in byssinosis, which is specific to cotton dust exposure and grain fever (*7*). Other microbial products may be inflammatory or immunomodulatory. These include (1,3) β-D-glucans, exotoxins from gram-positive and gram-negative bacteria, phytotoxins, heat shock proteins, and T-cell–activating superantigens (*7*). Further research is needed to determine what role these products play in respiratory disease.

Microorganisms

Infection

Farming, animal husbandry, and animal production environments can be reservoirs of human exposure to exotic and common infectious agents, resulting in zoonoses. For example, hog confinement workers can be at risk for acquiring swine influenza (*27*). Poultry workers, particularly those working with turkeys and ducks, are at risk for psittacosis caused by *Chlamydia psittacosis*. Veterinarians and zoo workers are also at risk for developing psittacosis. Q fever, resulting in atypical pneumonia, may result from aerosolization of the rickettsia *Coxiella burnetti* from infected sheep, goats, and cattle. Exposures occur in packing plants, dairies, stockyard facilities, and to sheep farmers and ranch hands during the birthing process (*27*). The incidence of Q fever was found to be higher than expected when surveillance of North Dakota sheep producers was undertaken (*28*). *C. burnetti* is a hardy and infectious organism, and aerosolized bacteria can be spread over a half mile, causing community outbreaks. *Mycobacterium bovis* is endemic in both wild and farm animals and can result in tuberculosis infection of veterinarians, farm workers, abattoir workers, and zookeepers (*4*).

Of great concern is the emergence of hantavirus pulmonary syndrome (HPS), which is associated with a significant fatality rate of 32–40%. This is primarily caused by the Sin Nombre virus, a single-stranded RNA hantavirus of the Bunyaviradae family. Documented cases have been associated with agricultural activities, including grain farmers and cleaning animal sheds. The exposure results from the aerosolization of rodent urine, saliva, and droppings found in contaminated dust in barns and storage facilities for farm equipment (*29*). The rodent vectors, primarily deer mice (*Peromyscus maniculatus*), cotton rat (*Sigmodon hispidus*), rice rat (*Oruzp,us palustris*), and the white-footed mouse (*Peromyscus leucopus*), are asymptomatic but are found in enclosed buildings. The initial febrile prodromal symptoms are nonspecific and similar to general viral syndrome but after 3–5 days may rapidly progress to pulmonary edema resulting in respiratory failure requiring mechanical ventilation. HPS has been most commonly associated with the Four Corners area of the Southwestern United States but may occur throughout the continental United States, Canada, Mexico, and Central and South America.

Toxic Gases

Nitrogen Oxides

Nitrogen oxides (NO_x), the cause of silo filler's disease, are formed during the fermentation of silage, with levels reaching concentrations of several hundred to several thousand parts per million (*7*). NO_x are poorly soluble and heavier than air and collect in pockets and depressions. Corn and other grain grown under drought conditions with heavy fertilization can produce extremely high levels of NO_x (*7*). NO_x gases are of low solubility, penetrating to the lower respiratory tract, and are severe respiratory irritants. Fermentation occurs within hours of filling a silo and NO_x may reach lethal levels within 12 hr; dangerous levels can persist for

Table 2. Selected current and recommended maximum agricultural and animal confinement exposures.

Hazard	OSHA PEL	NIOSH REL	ACGIH TLV	Animal confinement research[a]
Nuisance total dust	15 mg/m^3	NE	10 mg/m^3	
Nuisance hazard respirable dust	5 mg/m^3	NE	3 mg/m^3	
Grain dust	10 mg/m^3	4 mg/m^3	4 mg/m^3	
Organic dust	NE	NE	NE	2.4–2.5 mg/m^3
Respirable organic	NE	NE	NE	0.16–0.23 mg/m^3
Endotoxin	NE	NE	NE	640–1000 ng/m^3
Ammonia	50 ppm	25 ppm	25 ppm	7.5 ppm

NE, not established.
[a]Data from Donham et al. (*14*), Reynolds et al. (*15*), and Donham et al. (*16*).

2 weeks afterward. Silos should not be entered during this time without proper respiratory protection and only after running blowers for at least 30 min. Measurement of the NO_x prior to entry of the silo is recommended, even after ventilation (*30*). Acute, usually accidental, high-level exposure can be a cause of acute hemorrhagic pulmonary edema and death. Lower level exposure may produce transient pulmonary decompensation, but pulmonary disease can be a long-term sequela as a result of fibrotic scarring (*31*).

Animal Confinement Gases

Aside from the attendant health risks of organic dusts, high-density animal confinement facilities, and in particular swine confinement operations, generate high levels of gases as part of the byproducts of animal waste. These gases include hydrogen sulfide (H_2S), ammonia, carbon dioxide, and methane. The gases of primary concern are H_2S and ammonia. Accidental death due to H_2S asphyxiation and or cardiogenic pulmonary edema is rare but can occur in those swine or dairy confinement buildings with under-building manure pits (*32*). H_2S at low levels is a respiratory irritant and at higher levels a chemical asphyxiant. H_2S has a low odor threshold. It is easily detected by the "rotten-egg" smell at 0.13 ppm, a level well below the OSHA PEL of 10 ppm. At increasingly higher levels (above 150 ppm), olfactory paralysis occurs and the odor can no longer be detected. Pulmonary edema can occur at levels of 250 ppm and unconsciousness and death at 500 ppm. Agitation of manure, which occurs when manure pits are emptied, can release concentrations of H_2S as high as 1,000 ppm into the breathing zone of humans and animals.

Ammonia is a common gas found in animal and poultry confinement operations. Ammonia is a respiratory and mucous membrane irritant. It is very soluble and associated with upper airway irritation, sinusitis, chronic obstructive pulmonary conditions, and mucous membrane inflammation syndrome. This is discussed in more detail later in this review. Tolerance can develop with prolonged exposure, leading to fewer irritant symptoms with greater pulmonary exposure. Prolonged exposure to ammonia at levels below the PEL of 25 ppm has been linked to adverse health effects (*15,16*). Less consistent trends occur with ammonia exposure than with endotoxin exposure (*16*). It has been suggested that long-term exposure of > 2 hr/day for 6 years is associated with a variety of conditions, including sinusitis, mucous membrane inflammation syndrome, chronic bronchitis, and asthmalike syndrome (*8*). Recommendations have been made for exposure levels lower than the current recommended PELs and TLVs for ammonia, as well as dusts, endotoxins, and microorganisms (*14–16,22*) (Table 2).

Unlike H_2S, carbon dioxide and methane are simple asphyxiants and generally are not primary causes of adverse health effects. Carbon dioxide, produced by animal respiration, serves as an indirect indicator of ventilation, with acceptable concentrations below 5,000 ppm. Methane at concentrations > 5% is also a potential explosive hazard (*8*). Carbon monoxide is not generated from animal wastes but may reach high levels as a result of operating gasoline-powered pressure washers or kerosene heaters in poorly ventilated buildings. Toxic levels resulting in carbon monoxide poisoning can develop within 3–5 min. Even higher levels consistent with atmospheres immediately dangerous to life and health may develop at 30 min and result in coma, respiratory arrest, long-term neurologic complications, and death (*33*).

Manure pits and lagoons are anaerobic environments and considered to be immediately dangerous to life and health inside the confines of the enclosures. They also contain extremely high levels of H_2S, methane, ammonia, and carbon dioxide. A person may lose consciousness within seconds and collapse into the manure. Those entering to rescue the fallen individual without SCBA may also succumb. Multiple fatalities have occurred and continue to occur every several years throughout the country. The pits and lagoons should never be entered without a safety harness and properly functioning SCBA. Those that survive near-drowning in lagoons can develop dung lung, a polymicrobial-caused pneumonia (*8*).

Pesticides

Although there are well-recognized health effects of pesticides, particularly those affecting the central nervous and sympathetic/parasympathetic nervous systems, generally speaking and with notable exceptions, pesticides are not a cause of chronic pulmonary disease. For example, Paraquat, a restricted-use bipyridyl herbicide, is a well-characterized inducer of free radicals in lung tissue and the cause of pulmonary fibrosis in humans. Intoxication by the commonly used herbicide Roundup (glyphosphate) may be associated with the development of chemical pneumonitis. Organophosphates and carbamates, because of their effects on cholinesterase, produce bronchoconstriction but have no well-documented, long-term pulmonary effects in humans. Altogether, few pesticides other than those cited above are associated with the development of chronic or acute pulmonary disease.

Respiratory Illnesses and Syndromes

Agricultural respiratory conditions tend to have an overlapping spectrum (Figure 1). Also, respiratory symptoms caused by agricultural exposures are nonspecific and often mistaken for common viral or bacterial respiratory infections. Unless a careful occupational history is taken, the proper diagnosis may not be identified. Soluble gases such as ammonia, normally absorbed into mucous membranes of the upper airways, adsorb onto dust particles that can penetrate further into the lower respiratory tract than the gases would as a single entity. It is difficult to distinguish the separate adverse effects of gases and dusts, as they occur together in agricultural environments.

Hypersensitivity Pneumonitis

Several thermophilic actinomyces species, *Saccharaopolyspora rectivirgula* in particular, and certain *Aspergillus* fungi species, including *A. fumigatus* and *A. umbrosus*, have been associated with farmer's hypersensitivity pneumonitis (FHP), previously referred to as farmer's lung disease (*7*). These organisms are found in moldy hay, straw, and feed. FHP is a complex disease that has elements of an immunologic and cell-mediated allergic response that does not fit wholly into any of the four types of allergic reactions. Continued exposure to antigen in sensitized individuals may lead to an antigen-antibody complex formation suggesting a type III reaction and a late-phase cell-mediated response with granuloma formation compatible with a type IV reaction (*34*). As an initiating event (acute phase), high-level exposures to moldy dusts result in clinical effects symptomatically equivalent to ODTS but generally with radiographically demonstrable alveolar lung infiltrates and oxygen desaturation. More

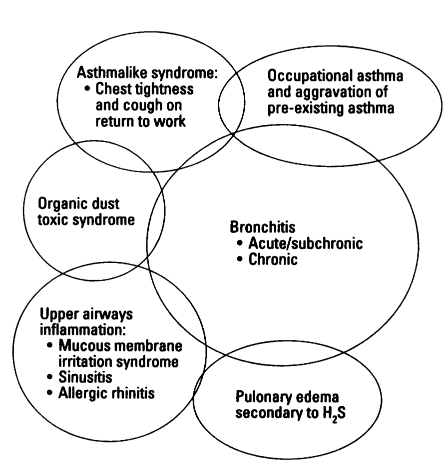

Figure 1. The spectrum of respiratory disease in swine confinement workers. Adapted from Von Essen and Donham (*69*).

commonly, repeated (subacute) exposures to relatively low levels of antigens in organic dusts lead to the insidious loss of pulmonary function. Pathologically, extensive and localized alveolar infiltrates of lymphocytes are noted in the initial phases of this disease, progressing to the formation of granuloma. However, as the disease progresses, chest X ray shows fibrotic changes in the lung fields. High-resolution chest computed tomography shows evidence of disease, including emphysema, earlier in the course of disease (*35*). In the chronic form of the disease, extensive lung fibrosis occurs (*36*). Antibodies to thermophilic bacteria and molds, termed serum precipitins, occur early in the course of the disease and are present in up to 90% of individuals with acute symptoms but tend to wane later in the course of disease. Asymptomatic exposed individuals also have positive serum precipitins, but this does not indicate actual disease. Estimates of prevalence, based upon positive serum precipitins, range from 5 to 20% with > 1% having the actual disease (*20*). According to the Canadian Centre for Occupational Health and Safety, perhaps as many as 2–10% of farm workers in Canada have FHP.

It is to be noted that prevalence of the disease varies according to climate. FHP is most common in cool and moist northern climates. Symptomatic attacks are more common in late winter or early spring when stored hay or grains are used to feed livestock. Extremely high levels of bacterial spores can be released from activities that raise high dust levels. Handling wet moldy hay or feed can release levels as high as 100×10^6 spores/g dust compared to 5×10^6 spores/g released from dry, properly stored hay and feed (*20*). If ventilation is inadequate, the spore content can be as high as $1,600 \times 10^6/m^3$. Using a bedding chopper to break up straw can increase the concentration by 50-fold. Interestingly, nonsmokers have a higher prevalence of FHP than smokers. Smoking, however, may result in a more insidious development of FHP resulting in a chronic form, as acute attack rates were lower and mortality significantly higher in smokers with FHP compared to nonsmokers with FHP (*37*). Once sensitization has occurred, continued exposure to low levels of antigen can lead to progressive irreversible pulmonary disease including emphysema. Other agricultural operations are associated with variants of FHP including poultry production, mushroom production, raising of birds, and many other operations that process vegetable and animal products.

Guidelines for the diagnosis of FHP have been published (*38*). The recognized criteria to establish the diagnosis include the following: *a*) the history and physical findings and pulmonary function tests indicate interstitial disease; *b*) the X-ray film is consistent with interstitial disease; *c*) there is an exposure to a recognized cause of FHP; and *d*) there is antibody to the antigen. If these criteria are met, pulmonary biopsy is not indicated. The American Thoracic Society Conference Report (*7*) nicely summarized FHP and included in the comments: *a*) FHP leads to progressive symptoms in at least one-third of those affected; *b*) FHP may be fatal if unrecognized; *c*) recurrences are an important determinant of clinical outcome; and *d*) emphysema is an important outcome of FHP (*7*). Clearly, early recognition of the sources of exposure and symptoms by farmers and their physicians is a key to prevention and control of this disease. Decreased exposure to molds and thermophilic bacteria can be accomplished by personal respiratory protection and work practices designed to decrease dust production and increase ventilation. These are discussed later in the prevention section.

Organic Dust Toxic Syndrome

Typical ODTS occurs as a result of exposure to mold-laden hays and grains (silo unloader's syndrome). ODTS cannot be distinguished from FHP by clinical symptoms. They both occur 4–8 hr after exposure and result in self-limited flulike illnesses consisting of chest tightness, shortness of breath, dry cough, fever, chills, myalgias, and fatigue. ODTS is often misdiagnosed as farmer's lung, which is the default diagnosis for many respiratory illnesses resulting from agricultural exposures, particularly if an adequate exposure history is not obtained and appropriate testing is not performed. Medical tests to distinguish the two conditions include complete pulmonary function tests, oxygen saturation, and chest radiography. It is probable that ODTS is a toxic reaction rather than an immune reaction. Endotoxin is the probable chief cause of inflammation but endotoxin-free grain extract can also contribute to a pulmonary inflammatory reaction (*39*). Unlike FHP, sensitization does not occur, and the condition is not progressive and resolves within several days. The concentration of molds and dust associated with ODTS is approximately 10 times greater than that associated with FHP (*7*). Of interest, this nonallergic acute respiratory inflammatory disease is highly prevalent in workers engaged in swine confinement operations and has been reported as high as 34% (*8*).

On the basis of my personal experience (SK) interviewing attendees at agricultural health fairs and performing clinical evaluations, there are many anecdotal reports of recurrent attacks with the individuals aware of the precipitating cause. A recent survey of attendees at an agricultural trade show identified symptoms consistent with ODTS in 36% of those evaluated. Symptoms were significantly associated with grain dust exposure. Grain sorghum was more strongly associated with respiratory symptoms than other grains (*40*). Environmental and work conditions associated with ODTS are similar to FHP and include uncapping silos, cleaning out old chicken coops, cleaning up moldy feed, breaking open moldy hay and straw bales, and swine confinement operations. ODTS is more common than FHP, particularly in swine confinement. Preventive measures are similar to those used to prevent FHP.

Other Respiratory Conditions

Animal confinement units have been associated with newly recognized pulmonary conditions such as mucous membrane inflammation syndrome and asthmalike syndrome. Mucous membrane inflammation syndrome consists of nasal, eye, and throat symptoms. Nasal lavage has demonstrated immunomodulatory effects including increased levels of interleukin-1α, and interleukin-1β, and interleukin-6 (*8*). It is the most commonly reported complex of symptoms in those exposed to dusts and gases. The symptoms of rhinitis have been reported to range from 20 to 50% (*7*).

Farmers and agricultural workers generally have a lower prevalence of diagnosed asthma than the general population, which is thought to be due to the healthy worker effect. Those that cannot tolerate the exposures and develop symptoms or illnesses tend to leave agricultural work. A recent asthma prevalence study from New Zealand reported lower prevalence rates than the general population (*41*). A study of French dairy farmers did not demonstrate an increase in asthma, although other respiratory symptoms were increased (*42*).

Asthmalike syndrome is associated with swine confinement workers and grain elevator operators, with acute symptoms reported in as many as 50% (*7*). The associated clinical symptoms of cough, chest tightness, wheeze, and dyspnea (air hunger) are identical to asthma but lack persistent airway inflammation, increased eosinophils on bronchoalveolar lavage, or significant pulmonary hyperresponsiveness. With this condition, the symptoms are more pronounced upon return to work after some time away from exposure, such as a weekend or vacation. This is similar to byssinosis in cotton-batting workers or metal-fume fever in welders. Diagnosis can be difficult, as there is only a small decrement in the FEV_1 that is temporary and may still be within the accepted normal values. Often the only method of documenting this is by comparing the postshift pulmonary function testing to the preshift pulmonary testing (cross-shift testing) (*23,24*). The cross-shift decrease in FEV_1 is generally less than 10% (*7*).

The prevalence of true occupational asthma in agriculture is unknown, varies from country to country, and is influenced by the types of commodities, work practices, and environmental conditions. Occupational asthma is rare in swine confinement but may be seen in those exposed to grain, cotton dust, and soybean dust.

Other more commonly recognized respiratory conditions are aggravated by organic dusts and gases associated with agricultural exposures. Individuals with preexisting asthma often do not tolerate working with grain dust or in animal confinement for more than relatively short periods of time. Symptoms of chronic bronchitis, as defined by productive cough for 3 months a year for at least 2 years, are increased in animal and grain production and grain elevator workers, with a symptom prevalence ranging from 25 to 50% (*7,8,43,44*). Chronic bronchitis symptoms are associated with endotoxin exposure (*5,45*). Swine confinement workers and grain and vegetable farmers have a higher prevalence of chronic bronchitis symptoms than the general population (*46,47*). Smoking in isolation is a major risk factor in the development of chronic bronchitis, but several studies have identified an additive if not synergistic effect with agricultural exposures (*42,43*).

Animal Confinement, Odors, and Community Health

Noxious odors emanating from animal confinement facilities and their manure storage lagoons are an increasingly contentious issue in rural and bordering suburban communities. Gases arising from the decomposition of manure, including H_2S, methane, and ammonia, are one part of the many volatile and semivolatile organic components of the odorant mix (*48*). Livestock wastes have as many as 168 volatile organic compounds. The most important compounds contributing to odors include ammonia, diacetyl, volatile fatty acids, phonols, *p*-cresole, indoles, and skatoles (*49*). Aside from these odorants and potential pulmonary irritants, bacteria, fungi, and fungal spores can be infective or allergenic components of aerosols arising from the storage lagoons. However, we are not aware of any human health studies or well-described case studies that specifically address this potentially important respiratory health issue. There are increased environmental regulations limiting or prohibiting the use of uncovered manure pits and lagoons that will decrease the noticeable odors throughout the surrounding area. The Minnesota Pollution Control Agency currently measures H_2S at the property boundaries as a proxy for animal confinement gases when evaluating odor complaints. Control methods are instituted if the levels are repeatedly above the state H_2S ambient air standard of 30 ppb (*50*).

Current studies have evaluated symptomatic health reports of residents living in the vicinity of swine confinement areas. Depression, fatigue, confusion, and anger were significantly higher among these persons (*51*). The other main health complaints consist of eye, nose, and throat irritation, headache, and drowsiness (*52*). One pilot study indicated that neighbors of swine confinement facilities had significantly higher rates of symptom clusters associated with inflammation of the respiratory tract (*53*). A recent population-based study consisting of a survey of health complaints in North Carolina showed statistically significant increased upper respiratory symptoms and cough in community members living near hog operations, as well as decreased quality of life. The symptoms mirror those found in occupational exposures, but accompanying environmental monitoring was not performed (*54*). The current reporting status does not allow a judgment regarding the significance of this potential threat to respiratory health. It is uncertain which gas or gases should be measured when assessing the air pollution effects from large animal confinement operations. Currently, studies looking into respiratory conditions resulting from environmental exposure to animal confinement gases are pending in several states. Research needs include further studies that address the appropriate environmental monitoring of gases with a prospective case–control assessment of pulmonary and upper airway evaluation accompanying the subjective symptom surveys. Efforts to determine dose–response relationships, similar to those suggested to exist in occupational exposure studies, should be made (*52*).

Prevention

The use of personal respiratory devices is limited in agricultural operations because they are hot and uncomfortable and are not routinely worn. NIOSH-approved two-strap dust and mist respirators are adequate for prevention when working in dusty and moldy conditions (*55*). Studies have shown that the two-strap masks were effective in preventing further attacks of FHP (*37*). Respirators decreased symptoms in a group of German farmers with occupational asthma but did not completely prevent symptoms or the development of increased airway resistance (*56*). Severely sensitized individuals with diseases such as FHP or exposure to much higher concentrations of dusts will need more sophisticated and expensive respiratory protection with a greater respiratory protection factor to prevent further pulmonary deterioration and acute pulmonary injury. A typical example is a powered air-purifying respirator with a face shield and helmet. Individuals with documented disease and abnormal pulmonary functions should have ongoing medical surveillance of pulmonary functions and symptoms to ensure that respiratory protection is adequate. Chemical cartridges are necessary for higher concentrations of organic vapors and ammonia and should be considered at concentrations higher than 7.5 ppm. Only SCBA or air-supplying respirators are adequate for anaerobic conditions or environments immediately dangerous to life and health due to high concentrations of noxious gases and vapors. It is essential to recognize that very important barriers to safe work practices are occupational stressors such as long hours and dire economic conditions, which have been recognized as deterrents for the consistent use of appropriate preventive measures, including personal protective equipment (*57*).

Engineering controls are preferable to long-term use of personal respiratory protection. Methods of control include decreasing dust generation by adding mist, adding vegetable oil to feed, sprinkling oil on the animals, and using wet methods to clean surfaces (*58*). The use of canola oil sprinkled in a swine room significantly decreased adverse respiratory effects in human subjects and concomitantly decreased dust, endotoxin levels, H_2S, and ammonia (*59,60*). Fats added to feeds in the form of canola oil, rapeseed, and mineral oil decreased dust levels by 35–60% in swine confinement buildings (*61*). Ventilation with proper mixing of air improves air quality by decreasing dust and gas levels. Mechanical ventilation is recommended, as natural ventilation is not reliable or adequate (*4*). An important method of decreasing exposure to toxic levels of gases and endotoxins is the storage of manure in an enclosed leak-proof structure outdoors. Concentrations of gases should be monitored periodically by the use of simple colorimetric tubes or direct-reading electronic monitors. In confined spaces with potentially lethal concentrations of gases that can rapidly change, such as silos with NO_x, multiple measurements with electronic direct-reading monitors should be obtained prior to fully opening the door and entering the space (*30*). Frequent use of disinfectants, wood shavings for bedding, and mechanical feeding systems have been associated with higher prevalence of respiratory disorders (*62,63*).

Newer methods of storing silage have decreased indoor exposure to molds and dusts. Bunkers, plastic-wrapped silage combined with outdoor storage, decrease exposure to dusts and molds. Capping silage with plastic sheeting decreases decay and mold growth. Harvesting and storing hay, straw, and grains with moisture content below 30–35% and adding urea as a preservative decreases mold and bacteria growth (*42,64*). Adding a quart of water to a bale of hay before chopping decreases dust release by as much as 85% (*65*).

An underused resource in agricultural respiratory disease prevention is the rural health care provider. It has been recognized that health-care providers have had inadequate training in agricultural health and self-report inadequacies in competency in diagnosing exposure to noxious gases (*66,67*). Increased knowledge on the part of health-care providers of work practices and environmental exposures that have the potential to cause adverse respiratory health effects is an important component of prevention of agricultural respiratory disease (*68*).

Accessible, accurate, and less-expensive devices to directly monitor the concentrations of dust, gases, and endotoxins in animal confinement operations need to be more consistently utilized. Increased routine use of air monitoring of hazardous gases is necessary to identify toxic levels. Respiratory protection with appropriate protection factors can then be instituted. Dose–response relationships between organic dust and endotoxin concentrations and adverse pulmonary effects have been demonstrated in various studies. With this understanding, it is essential to decrease the production of gases and dusts and provide improved ventilation technology. The ability to retrofit these controls upon existing structures at an affordable cost is very important. If cost is not considered, a significant number of producers who cannot afford to build state-of-the-art animal confinement buildings will not benefit from technologic advances.

Summary

It is clear that present-day agricultural exposures to dusts and gases are associated with acute and chronic respiratory diseases and syndromes. Improved engineering controls have decreased exposures to dusts during field operations through the use of enclosed cabs and air filtration. Consequences of the evolution in increasingly larger animal confinement operations include the increased extent and duration of exposure to biologically active respiratory inflammatory compounds. Improved respiratory hazard controls will be essential to decrease the health risks to farmers and other agricultural workers. For the present, increased and more universal use of personal respiratory protection during high-exposure procedures is necessary to decrease respiratory exposures to inhaled dusts and gases. Currently, smaller production agriculture operations with 10 or fewer employees or individual owner/principle operators generally do not undergo medical surveillance for respirator use or the detection of pulmonary deterioration. Further occupational safeguards will be essential to protect the agricultural workers exposed to these potent respiratory toxins. These efforts will include improved medical surveillance and the establishment of TLVs and PELs that adequately protect the health of those working in agriculture.

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